

**PRELIMINARY AMENDMENT**

U.S. Appln. No.: 10/520,660

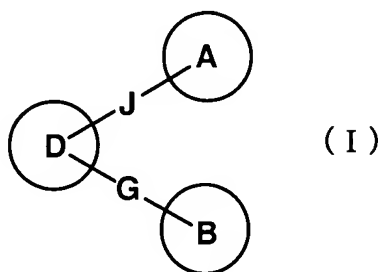
**AMENDMENTS TO THE CLAIMS**

**This listing of claims will replace all prior versions and listings of claims in the application:**

**LISTING OF CLAIMS:**

**Please cancel claim 45.**

1. (Original) A compound of formula (I):



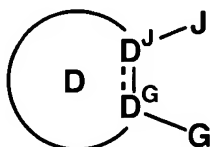
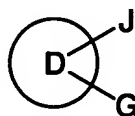
wherein ring A, ring B, and ring D each independently represents a cyclic group which may be substituted;

J represents a bond or a spacer having 1 to 8 atoms in its main chain; and

G represents a bond or a spacer having 1 to 4 atoms in its main chain;

or a salt thereof.

2. (Original) The compound according to claim 1, wherein



wherein  $D^J$  and  $D^G$  each independently represents a carbon atom or a nitrogen atom; and

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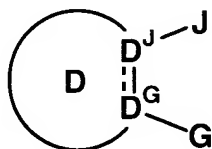
---- represents a single bond or a double bond, and  
when == represents a double bond,  $D^J$  and  $D^G$  each represents a carbon atom.

3. (Original) The compound according to claim 2, wherein ring D is a carbocyclic ring which may be substituted.

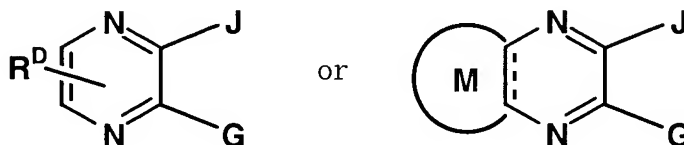
4. (Original) The compound according to claim 2, wherein ring D is a heterocyclic ring which may be substituted.

5. (Original) The compound according to claim 4, wherein the heterocyclic ring is a 3- to 15-membered monocyclic, bicyclic or tricyclic heterocyclic ring having 1 to 4 nitrogen atoms, 1 or 2 oxygen atoms and/or 1 or 2 sulfur atoms as a hetero atom(s).

6. (Original) The compound according to claim 2, wherein

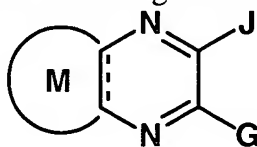


is



wherein  $R^D$  represents a substituent of ring D; and  
M represents a 3- to 11-membered monocyclic or bicyclic cyclic group which may be substituted.

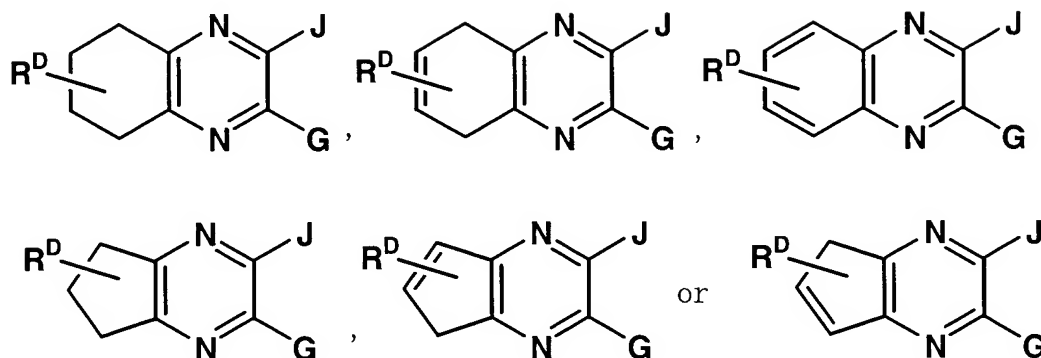
7. (Original) The compound according to claim 6, wherein



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wherein  $R^D$  has the same meaning as described in claim 6.

8. (Original) The compound according to claim 1, wherein ring A is a carbocyclic ring which may be substituted.

9. (Original) The compound according to claim 1, wherein ring A is a heterocyclic ring which may be substituted.

10. (Original) The compound according to claim 8, wherein the carbocyclic ring is a C3-15 monocyclic, bicyclic or tricyclic carbocyclic ring.

11. (Original) The compound according to claim 9, wherein the heterocyclic ring is a 3- to 15-membered monocyclic, bicyclic or tricyclic heterocyclic ring having 1 to 4 nitrogen atoms, 1 or 2 oxygen atoms and/or 1 or 2 sulfur atoms as a hetero atom(s).

12. (Original) The compound according to claim 10, wherein the carbocyclic ring is a benzene ring or a naphthalene ring.

13. (Original) The compound according to claim 11 wherein the heterocyclic ring is a pyridine ring, a pyrazole ring, a dioxaindane ring or a benzodioxane ring.

14. (Original) The compound according to claim 1, wherein ring B is a carbocyclic ring which may be substituted.

15. (Original) The compound according to claim 1, wherein ring B is a heterocyclic ring which may be substituted.

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16. (Original) The compound according to claim 14, wherein the carbocyclic ring is a C3-15 monocyclic, bicyclic or tricyclic carbocyclic ring.

17. (Original) The compound according to claim 15, wherein the heterocyclic ring is a 3- to 15-membered monocyclic, bicyclic or tricyclic heterocyclic ring having 1 to 4 nitrogen atoms, 1 or 2 oxygen atoms and/or 1 or 2 sulfur atoms as a hetero atom(s).

18. (Original) The compound according to claim 16, wherein the carbocyclic ring is a C3-8 monocyclic carbocyclic ring.

19. (Original) The compound according to claim 17, wherein the heterocyclic ring is a 3- to 8-membered monocyclic heterocyclic ring having 1 to 4 nitrogen atoms, 1 or 2 oxygen atoms and/or 1 or 2 sulfur atoms as a hetero atom(s).

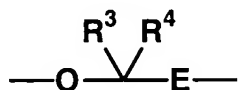
20. (Original) The compound according to claim 18, wherein the carbocyclic ring is a benzene ring.

21. (Original) The compound according to claim 19, wherein the heterocyclic ring is a pyridine ring or a thiophene ring.

22. (Original) The compound according to claim 1, wherein J is a spacer having 1 to 8 atoms in its main chain and containing at least one oxygen atom.

23. (Original) The compound according to claim 22, wherein the oxygen atom binds to ring D.

24. (Original) The compound according to claim 22, wherein J is



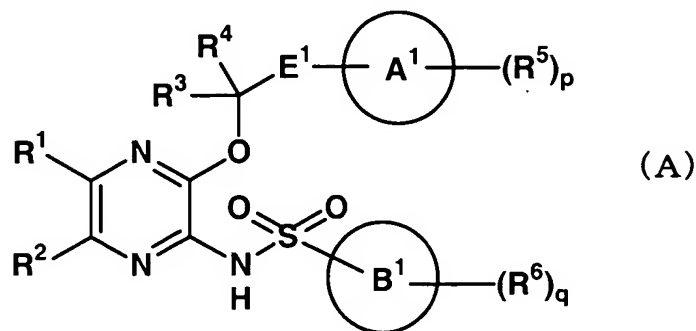
wherein  $\text{R}^3$  and  $\text{R}^4$  each independently represents hydrogen or C1-8 alkyl; and E represents a bond or a spacer having 1 to 6 atoms in its main chain.

25. (Original) The compound according to claim 24, wherein  $\text{R}^3$  and  $\text{R}^4$  each independently represents hydrogen or methyl.

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26. (Original) The compound according to claim 24, wherein E is a bond,
27. (Original) The compound according to claim 24, wherein E is a spacer having 1 to 6 atoms in its main chain.
28. (Original) The compound according to claim 27, wherein E is C1-4 alkylene or C1-3 alkyleneoxy.
29. (Original) The compound according to claim 28, wherein E is methylene or methylenoxy.
30. (Original) The compound according to claim 1, wherein G is a spacer having 1 to 4 atoms in its main chain and containing at least one nitrogen atom.
31. (Original) The compound according to claim 30, wherein G is  $\text{-NR}^{\text{T1-}}$ ,  $\text{-NR}^{\text{T1-}}$  $\text{SO}_2\text{-}$ ,  $\text{-NR}^{\text{T1-}}\text{CO-}$ ,  $\text{-NR}^{\text{T1-}}\text{CO-NR}^{\text{T2-}}$ ,  $\text{-NR}^{\text{T1-}}\text{SO}_2\text{-NR}^{\text{T2-}}$ ,  $\text{-NR}^{\text{T1-}}\text{COO-}$ ,  $\text{-NR}^{\text{T1-}}\text{O-}$ ,  $\text{-NR}^{\text{T1-}}\text{NR}^{\text{T2-}}$ ,  $\text{-NR}^{\text{T1-}}\text{W-}$ ,  $\text{-SO}_2\text{-NR}^{\text{T1-}}$ ,  $\text{-CO-NR}^{\text{T1-}}$ ,  $\text{-OCO-NR}^{\text{T1-}}$ ,  $\text{-O-NR}^{\text{T1-}}$  or  $\text{W-NR}^{\text{T1-}}$ , wherein W represents a bivalent C1-3 aliphatic hydrocarbon group which may be substituted;  $\text{R}^{\text{T1}}$  and  $\text{R}^{\text{T2}}$  each independently represents hydrogen, C1-8 alkyl which may be substituted, C2-8 alkenyl which may be substituted, C2-8 alkynyl which may be substituted or a 3- to 8-membered cyclic group which may be substituted.
32. (Original) The compound according to claim 31, wherein G is  $\text{-NH-SO}_2\text{-}$ .
33. (Original) The compound according to claim 1, wherein the compound is a compound of formula (A):



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wherein  $R^1$  and  $R^2$  each independently represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) halogen, (6) cyano, (7) nitro, (8)  $-\text{CONR}^7\text{R}^8$ , (9)  $-\text{COOR}^9$ , (10) Cyc1 or (11) C1-8 alkyl substituted with 1 to 5 groups selected from (a)  $-\text{CONR}^7\text{R}^8$ , (b)  $-\text{COOR}^9$ , (c)  $-\text{OR}^{10}$ , (d)  $-\text{NR}^{11}\text{R}^{12}$ , (e) halogen, and (f) Cyc1; or

$R^1$  and  $R^2$  are taken together to represent C3-4 alkylene,  $-\text{CH}=\text{CH}-\text{CH}_2-$ ,  $-\text{CH}_2-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$  or  $-\text{CH}=\text{CH}-\text{CH}_2-\text{CH}_2-$ , wherein the carbocyclic ring to be formed may be substituted with C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, C1-8 alkoxy, halogen, cyano, nitro or hydroxyl, wherein  $R^7$  and  $R^8$  each independently represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) Cyc2, (6)  $-\text{OR}^{13}$  or (7) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1 to 5 groups selected from (a)  $-\text{OR}^{13}$ , (b)  $-\text{NR}^{14}\text{R}^{15}$ , (c)  $-\text{NR}^{16}\text{COR}^{17}$ , (d) halogen, (e)  $\text{CF}_3$ , and (f) Cyc2; or

$R^7$  and  $R^8$  are taken together with the adjacent nitrogen atom to represent a 3- to 8-membered monocyclic heterocyclic ring having at least one nitrogen atom as a hetero atom(s) and 0 to 3 nitrogen atoms, 0 to 1 oxygen atom and/or 0 to 1 sulfur atom as an other hetero atom(s), wherein the heterocyclic ring may be substituted with (a) C1-8 alkyl, (b) halogen, (c) hydroxyl, or (d) C1-8 alkyl substituted with hydroxyl;

$R^{13}$  to  $R^{17}$  each independently represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) Cyc1, or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc1;

$R^9$  to  $R^{12}$  each independently represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) Cyc1, or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc1;

Cyc1 represents a C3-15 monocyclic, bicyclic or tricyclic carbocyclic ring or a 3- to 15-membered monocyclic, bicyclic or tricyclic heterocyclic ring having 1 to 4 nitrogen atoms, 1 or 2 oxygen atoms and/or 1 or 2 sulfur atoms as a hetero atom(s), wherein Cyc1 may be substituted with 1 to 5 of  $R^{18}$ ;

$R^{18}$  represents (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) halogen, (5) cyano, (6) nitro, (7) trifluoromethyl, (8) trifluoromethoxy, (9)  $-\text{OR}^{19}$ , (10)  $-\text{SR}^{20}$ , (11)  $-\text{NR}^{21}\text{R}^{22}$ , (12)  $-\text{COR}^{23}$ , (13)  $-\text{COOR}^{24}$ , (14)  $-\text{NR}^{25}\text{COR}^{26}$ , (15)  $-\text{CONR}^{27}\text{R}^{28}$ , (16) Cyc2, or (17) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1 to 5 groups selected from (a) halogen, (b) cyano, (c) nitro, (d) trifluoromethyl, (e) trifluoromethoxy, (f)  $-\text{OR}^{19}$ , (g)  $-\text{SR}^{20}$ , (h)  $-\text{NR}^{21}\text{R}^{22}$ , (i)  $-\text{COR}^{23}$ , (j)  $-\text{COOR}^{24}$ , (k)  $-\text{NR}^{25}\text{COR}^{26}$ , (l)  $-\text{CONR}^{27}\text{R}^{28}$ , and (m) Cyc2;

$R^{19}$  to  $R^{28}$  each independently represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) Cyc2, or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc2;

Cyc2 represents a C3-8 monocyclic carbocyclic ring or a 3- to 8-membered monocyclic heterocyclic ring having 1 to 4 nitrogen atoms, 1 or 2 oxygen atoms and/or 1 or 2 sulfur atoms as a hetero atom(s), wherein Cyc2 may be substituted with 1 to 5 of  $R^{29}$ ;

$R^{29}$  represents (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) halogen, (5) cyano, (6) nitro, (7) hydroxyl, (8) trifluoromethyl, (9) trifluoromethoxy, or (10)  $-\text{OR}^{100}$ ;

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R<sup>100</sup> represents C1-8 alkyl;

R<sup>3</sup> and R<sup>4</sup> each independently represents hydrogen or C1-8 alkyl;

E<sup>1</sup> represents a bond or C1-6 alkylene, wherein a carbon atom in the alkylene group may be substituted with oxygen, sulfur, or -NR<sup>30</sup>;

R<sup>30</sup> represents (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) phenyl, or (5) C1-8 alkyl substituted with phenyl;

ring A<sup>1</sup> represents a C3-15 monocyclic, bicyclic or tricyclic carbocyclic ring or a 3- to 15-membered monocyclic, bicyclic or tricyclic heterocyclic ring having 1 to 4 nitrogen atoms, 1 or 2 oxygen atoms and/or 1 or 2 sulfur atoms as a hetero atom(s);

R<sup>5</sup> represents (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) halogen, (5) cyano, (6) nitro, (7) trifluoromethyl, (8) trifluoromethoxy, (9) -OR<sup>31</sup>, (10) -NR<sup>32</sup>R<sup>33</sup>, (11) -NR<sup>34</sup>COR<sup>35</sup>, (12) Cyc3, or (13) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1 to 5 groups selected from (a) halogen, (b) cyano, (c) nitro, (d) trifluoromethyl, (e) trifluoromethoxy, (f) -OR<sup>31</sup>, (g) -NR<sup>32</sup>COR<sup>33</sup>, (h) -NR<sup>34</sup>COR<sup>35</sup>, and (i) Cyc3;

R<sup>31</sup> to R<sup>35</sup> each independently represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) Cyc3, or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1 to 5 groups selected from (a) Cyc3, (b) -OR<sup>36</sup> and (c) -NR<sup>37</sup>R<sup>38</sup>;

R<sup>36</sup> to R<sup>38</sup> each independently represents (1) hydrogen, (2) C1-8 alkyl, (3) -OR<sup>39</sup>, or (4) -NR<sup>40</sup>R<sup>41</sup>;

R<sup>39</sup> to R<sup>41</sup> each independently represents hydrogen or C1-8 alkyl;

Cyc3 represents a C3-8 monocyclic carbocyclic ring or a 3- to 8-membered monocyclic heterocyclic ring having 1 to 4 nitrogen atoms, 1 or 2 oxygen atoms and/or 1 or 2 sulfur atoms as a hetero atom(s);

ring B<sup>1</sup> represents a C3-15 monocyclic, bicyclic or tricyclic carbocyclic ring or a 3- to 15-membered monocyclic, bicyclic or tricyclic heterocyclic ring having 1 to 4 nitrogen atoms, 1 or 2 oxygen atoms and/or 1 or 2 sulfur atoms as a hetero atom(s);

R<sup>6</sup> represents (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) halogen, (5) cyano, (6) nitro, (7) trifluoromethyl, (8) trifluoromethoxy, (9) -OR<sup>42</sup>, (10) -NR<sup>43</sup>R<sup>44</sup>, (11) -SR<sup>101</sup>, (12) -SO<sub>2</sub>R<sup>102</sup>, (13) -COR<sup>103</sup>, (14) -COOR<sup>104</sup>, (15) Cyc2, or (16) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1 to 5 groups selected from (a) -COOR<sup>104</sup>, (b) -NR<sup>105</sup>COR<sup>106</sup>, and (c) Cyc2;

R<sup>42</sup> to R<sup>44</sup> and R<sup>101</sup> to R<sup>106</sup> each independently represents (1) hydrogen, (2) C1-8 alkyl, (3) Cyc2, or (4) -COR<sup>107</sup>, or (5) C1-8 alkyl substituted with 1 to 5 halogen atoms;

R<sup>107</sup> represents C1-8 alkyl; and

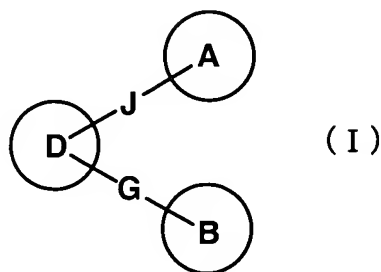
p and q each independently represents 0 or an integer of 1 to 5.

34. (Original) A prodrug for the compound according to claim 1.

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35. (Original) A pharmaceutical composition which comprises the compound of formula (I):



wherein ring A, ring B, and ring D each independently represents a cyclic group which may be substituted; J represents a bond or a spacer having 1 to 8 atoms in its main chain; and G represents a bond or a spacer having 1 to 4 atoms in its main chain; or a salt thereof.

36. (Original) The pharmaceutical composition according to claim 35, which is a chemokine receptor antagonist.

37. (Original) The pharmaceutical composition according to claim 36, wherein the chemokine receptor is CCR4.

38. (Original) The pharmaceutical composition according to claim 37, which is a preventive and/or therapeutic agent for CCR4-mediated diseases.

39. (Original) The pharmaceutical composition according to claim 38, wherein the CCR4-mediated diseases are inflammatory and/or allergic diseases, metabolism and/or endocrine system diseases, cancer diseases or infections.

40. (Original) The pharmaceutical composition according to claim 39, wherein the CCR4-mediated diseases are inflammatory and/or allergic diseases.

41. (Original) The pharmaceutical composition according to claim 40, wherein the inflammatory and/or allergic diseases are respiratory diseases or dermatosis.

42. (Original) The pharmaceutical composition according to claim 41, wherein the respiratory diseases are asthma.



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43. (Original) The pharmaceutical composition according to claim 41, wherein the dermatosis is atopic dermatitis.

44. (Original) A method for preventing and/or treating CCR4-mediated diseases in a mammal, which comprises administering to a mammal an effective amount of the compound according to claim 1 or a salt thereof.

45. (canceled) Use of the compound according to claim 1 or a salt thereof for the manufacture of a preventive and/or therapeutic agent for CCR4-mediated diseases.

46. (Original) A pharmaceutical composition which comprises: a preventive and/or therapeutic agent for CCR4-mediated diseases, which comprises the compound according to claim 1 or a salt thereof as an active ingredient; and one or at least two medicaments selected from a bronchodilator drug, a steroid drug, a non-steroidal antiinflammatory drug, a leukotriene receptor antagonist, a phosphodiesterase inhibitor, an immunosuppressant, an anti-allergic drug, a mediator-release inhibitor, an antihistamine drug, a metabolism promoter and/or a chemokine inhibitor.

47. (Original) The pharmaceutical composition according to claim 35, which is an inhibitor of effector cell function.

48. (Original) The pharmaceutical composition according to claim 47, which is an inhibitor of cell migration function.

49. (Original) The pharmaceutical composition according to claim 35, which is a TNF $\alpha$  regulator.